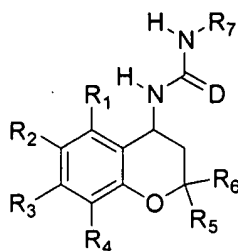


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CLAIMS

1. Benzopyran derivatives of the general formula



(I)

wherein :

D represents S or O;

10 R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, halogen, C<sub>1-6</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, hydroxy, C<sub>1-6</sub>-alkoxy, C<sub>1-6</sub>-alkoxy-C<sub>1-6</sub>-alkyl, nitro, amino, cyano, cyanomethyl, perhalomethyl, C<sub>1-6</sub>-monoalkyl- or dialkylamino, sulfamoyl, C<sub>1-6</sub>-alkylthio, C<sub>1-6</sub>-alkylsulfonyl, C<sub>1-6</sub>-alkylsulfinyl, formyl, C<sub>1-6</sub>-alkylcarbonylamino, R<sub>8</sub>arylthio, R<sub>8</sub>arylsulfinyl, R<sub>8</sub>arylsulfonyl, C<sub>1-6</sub>-alkoxycarbonyl, C<sub>1-6</sub>-alkoxycarbonyl-C<sub>1-6</sub>-alkyl, carbamoyl, carbamoylmethyl, C<sub>1-6</sub>-monoalkyl- or dialkylaminocarbonyl, C<sub>1-6</sub>-monoalkyl- or dialkylaminothiocarbonyl, ureido, C<sub>1-6</sub>-monoalkyl- or dialkylaminocarbonylamino, thioureido, C<sub>1-6</sub>-monoalkyl- or dialkylaminothiocarbonylamino, C<sub>1-6</sub>-monoalkyl- or dialkylaminosulfonyl, carboxy, carboxy-C<sub>1-6</sub>-alkyl, acyl, R<sub>8</sub>aryl, R<sub>8</sub>aryl-C<sub>1-6</sub>-alkyl, R<sub>8</sub>aryloxy;

20

R<sub>5</sub> and R<sub>6</sub> are each independently hydrogen, C<sub>1-6</sub>-alkyl or, R<sub>5</sub> and R<sub>6</sub> taken together with the carbon atom to which they are attached form a 3- to 6-membered carbocyclic ring;

25

R<sub>7</sub> is 2-, 3- or 4-pyridyl optionally mono- or polysubstituted by R<sub>1</sub> or

R<sub>7</sub> is 2- or 3-thienyl optionally mono- or polysubstituted substituted by R<sub>1</sub> or

R<sub>7</sub> is phenyl mono- or polysubstituted by R<sub>1</sub> with the exception of R<sub>7</sub> representing C<sub>6</sub>H<sub>5</sub>;

5

R<sub>8</sub> is hydrogen, halogen, C<sub>1-6</sub>-alkyl, C<sub>3-8</sub>-cycloalkyl, hydroxy, C<sub>1-6</sub>-alkoxy, nitro, amino, cyano, cyanomethyl, perhalomethyl;

10 or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture or any polymorphic and tautomeric form.

2. A benzopyran derivative according to claim 1 wherein D represents S.

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3. A benzopyran derivative according to claim 1 or 2 selected from :

R/S-4-(3-Chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,

20 R/S-6-Chloro-4-(3-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

R/S-4-(4-Chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,

25 R/S-6-Chloro-4-(4-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

R/S-6-Bromo-4-(4-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

30 R/S-4-(3-Cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,

R/S-6-Chloro-4-(3-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

- R/S-6-Bromo-4-(3-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,
- R/S-4-(4-Cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,
- 5 R/S-6-Chloro-4-(4-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,
- R/S-6-Bromo-4-(4-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,
- R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(3-
- 10 nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,
- R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(3-
- nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,
- R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(4-
- nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,
- 15 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(4-
- nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,
- R/S-4-(3-Chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,
- R/S-6-Chloro-4-(3-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-
- 20 dimethyl-2*H*-1-benzopyran,
- R/S-4-(4-Chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,
- R/S-6-Chloro-4-(4-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-
- dimethyl-2*H*-1-benzopyran,
- 25 R/S-6-Bromo-4-(4-chlorophenylaminothiocarbonylamino)-3,4-dihydro-2,2-
- dimethyl-2*H*-1-benzopyran,
- R/S-4-(3-Cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,
- R/S-6-Chloro-4-(3-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-
- 30 dimethyl-2*H*-1-benzopyran,

- R/S-6-Bromo-4-(3-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,  
 R/S-4-(4-Cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,  
 5 R/S-6-Chloro-4-(4-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,  
 R/S-6-Bromo-4-(4-cyanophenylaminothiocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,  
 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(3-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 10 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(3-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(4-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 15 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(4-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(4-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(4-nitrophenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 20 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(3-trifluoromethylphenylaminothiocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(2-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 25 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(2-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(3-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(3-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 30 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(3-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,

- R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(3-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(4-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 5 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(4-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(4-methoxyphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(2-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 10 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(2-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(2-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 15 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(3-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(3-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(3-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 20 R/S-3,4-Dihydro-2,2-dimethyl-6-fluoro-4-(4-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-6-Chloro-3,4-dihydro-2,2-dimethyl-4-(4-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 25 R/S-6-Bromo-3,4-dihydro-2,2-dimethyl-4-(4-methylphenylaminocarbonylamino)-2*H*-1-benzopyran,  
 R/S-4-(2-Chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,  
 R/S-6-Chloro-4-(2-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,  
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R/S-6-Bromo-4-(2-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

R/S-4-(3-Chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,

5 R/S-6-Chloro-4-(3-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

R/S-6-Bromo-4-(3-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

10 R/S-4-(4-Chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-6-fluoro-2*H*-1-benzopyran,

R/S-6-Chloro-4-(4-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran,

R/S-6-Bromo-4-(4-chlorophenylaminocarbonylamino)-3,4-dihydro-2,2-dimethyl-2*H*-1-benzopyran.

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4. Benzopyran derivatives according to any one of the preceding claims, for use as openers of the  $K_{ATP}$ -regulated potassium channels.

20 5. A pharmaceutical composition comprising a benzopyran derivative according to any one of the preceding claims or pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base or any optical isomer or mixture of optical isomers, including a racemic mixture or any tautomeric form together with one or more pharmaceutically acceptable carriers or diluents.

25 6. A pharmaceutical composition for use in the treatment of diseases of the endocrinological system such as hyperinsulinaemia and diabetes comprising a benzopyran derivative according to any one of the preceding benzopyran derivative claims or a pharmaceutical acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of

optical isomers, including a racemic mixture, or any tautomeric form together with a pharmaceutically acceptable carrier or diluent.

5 7. The pharmaceutical composition according to any one of the claims 5 or 6 in the form of an oral dosage unit or parental dosage unit.

10 8. A pharmaceutical composition according to any one of the claims 5 or 6 wherein said benzopyran derivative is administered as a dose in a range from about 0.05 to 1000, preferably from about 0.1 to 500 and especially in the range from 50 to 200 mg per day.

15 9. A benzopyran derivative according to any one of the preceding benzopyran derivative claims or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for therapeutic use.

20 10. A benzopyran derivative according to any one of the preceding benzopyran derivative claims or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for therapeutic use in the treatment of diseases of the endocrinological system, such as hyperinsulinaemia and diabetes.

25 11. The use of a benzopyran derivative according to any one of the preceding compound claims or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form as a medicament.

12. The use of a benzopyran derivative according to any of the preceding compound claims for preparing a medicament.

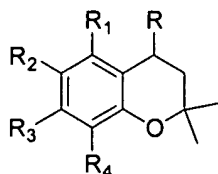
13. The use of a benzopyran derivative according to any one of the preceding benzopyran derivative claims or a pharmaceutically acceptable salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture, or any tautomeric form for the preparation of a medicament for the treatment of diseases of the endocrinological system, such as hyperinsulinaemia and diabetes.

14. A method of treating diseases of the endocrinological system, such as hyperinsulinaemia and diabetes in a subject in need thereof comprising administering an effective amount of a benzopyran derivative according to any one of the preceding benzopyran derivative claims to said subject.

15. A process for the manufacture of a medicament, particular to be use in the treatment of diseases of the endocrinological system, such as hyperinsulinaemia and diabetes which process comprising bringing a compound of formula (I) according to any one of the preceding compound claims 1 or a pharmaceutically acceptable salt thereof into a galenic dosage form.

16. A method of preparing a benzopyran derivative of formula (I) which comprises :

- reacting a compound of formula (II)



(II)



wherein R represents  $\text{NH}_2$  and  $\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$  and  $\text{R}_4$  are defined as for formula (I) with an isothiocyanate of formula (III)



wherein D represents S or O and  $\text{R}_7$  is defined as for formula (I), to form a benzopyran derivative of formula (I); or

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- reacting a compound of formula (II) wherein R represents  $\text{-N}=\text{C}=\text{S}$  and  $\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$  and  $\text{R}_4$  are defined as for formula (I) with an amine of formula (IV)



wherein  $\text{R}_7$  is defined as for formula (I), to form a benzopyran derivative of formula (I).